UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,567	11/12/2003	James L. Sackrison	DIA1001US	6918

9561 7590 12/03/2004

POPOVICH, WILES & O'CONNELL, PA
650 THIRD AVENUE SOUTH
SUITE 600
MINNEAPOLIS, MN 55402

EXAMINER	
VENCI, DAVID J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 12/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/706,567	SACKRISON ET AL.	
	Examiner	Art Unit	
	David J Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/5/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 15-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the recitation of "wherein the vitamin D binding proteins are not removed from the sample" is indefinite because it is not clear during which step in the method "vitamin D binding proteins are not removed from the sample" or whether "vitamin D binding proteins are not removed from the sample" during step (a) or step (b) or both. The recitation of "wherein the vitamin D binding proteins are not removed from the sample", although supported in the Summary of the Invention (see p. 2, lines 30-31), does not appear to have support in Protocol 1 or Protocol 2 of the Detailed Description of the Invention (see pp. 7-8). In both Protocol 1 and Protocol 2, the magnetic particles bearing vitamin D are removed/washed from the sample. Clarification is necessary.

In claims 15-19, the recitation of "a 22-carboxylic acid derivative of 25-hydroxy-vitamin D" appears to lack antecedent support in the specification. Furthermore, the recitation of "a 22-carboxylic acid derivative of 25-hydroxy-vitamin D" is indefinite because it is not clear what vitamin D compound is "a 22-carboxylic acid derivative of 25-hydroxy-vitamin D" or the chemical

structure of such a compound or how "a 22-carboxylic acid derivative of 25-hydroxy-vitamin D" is linked to a 2,2'-(Ethylenedioxy)diethylamine linker.

Claims 16-19 are indefinite because it is not clear how a polyethylene glycol linker, or a dimethyl adipimidate linker, or a diamino cyclohexane linker, or a diamino C_3- to C_{12}- linker are linked to ABEI and "a 22-carboxylic acid derivative of 25-hydroxy-vitamin D."

In claims 18-19, the recitation of "diamino" is indefinite because it is not clear what amino substitutions are required for a "diamino" substitution. It is not clear how a "diamino" group is incorporated into a cyclohexane linker, or how a "diamino" group is incorporated into a carbon chain linker.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Armbruster et al. (US 6,787,660) in view of Romelli et al. (US 5,382,530).

Armbruster et al. describe a method for assaying 25-hydroxy-vitamin D (see Title) in a sample of blood or blood components (see col. 6, lines 38-42) comprising the steps of: determining the

concentration of 25-hydroxy-vitamin D in the sample wherein the vitamin D binding proteins are not removed from the sample (see Fig. 6) (col. 9, lines 1-6).

Armbruster et al. do not teach the step of lowering the pH of the sample to 5.5 or less to dissociate 25-hydroxy-vitamin D from vitamin D binding proteins.

However, Romelli et al. teach the step of varying the pH of a sample (see col. 7, lines 35-39) as a means for dissociating vitamins (see col. 4, line 4) from their respective binding proteins.

Therefore, it would have been obvious for a person of ordinary skill in the art at the time of invention to use the method for assaying 25-hydroxy-vitamin D, as taught by Armbruster et al., with the step of lowering the pH of the sample, as taught by Romelli et al., because Romelli et al. teach that varying pH causes ligands, including vitamins, to dissociate from their respective binding proteins, which allows these previously-bound ligands to be present during all measurement stages, which consequently results in higher assay sensitivity (see col. 4, lines 38-39) and simplification of operating procedures as compared to the prior art extractions (see col. 4, lines 56-58).

With respect to claims 2-7, it would have been obvious to a person of ordinary skill in the art to lower the pH of the blood sample to pH 5.5 or less in order to cause dissociation of 25-hydroxyvitamin D from vitamin D binding protein, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. See *In re Aller,* 105 USPQ 233 (CCPA 1955).

With respect to claims 8-9, Romelli et al. teach the use of citrate buffers to lower the pH of a sample (see Table VI).

With respect to claim 10, Armbruster et al. teach a method for assaying 25-hydroxy-vitamin D wherein the concentration is determined by immunoassay (see Fig. 7).

With respect to claim 11, Armbruster et al. teach a method for assaying 25-hydroxy-vitamin D wherein the sample is serum or plasma (see col. 6, lines 38-42).

With respect to claim 12, the step of varying the pH of a sample as a means for dissociating vitamins from their respective binding proteins, as taught by Romelli et al., necessarily does not form a precipitate, and would be so recognized by persons of ordinary skill in the art.

With respect to claim 13, Armbruster et al. teach a method for assaying 25-hydroxy-vitamin D wherein a vitamin D tracer is used (see Abstract).

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Armbruster et al. (US 6,787,660) in view of Romelli et al. (US 5,382,530) as applied to claims 1, 10 and 13, and further in view of Schroeder et al., 57 METHODS ENZYMOL. 424 (1978).

Armbruster et al. and Romelli et al. teach a method for assaying 25-hydroxy-vitamin D as substantially described supra. Armbruster et al. and Romelli et al. do not teach the use of an ABEI tracer.

However, Schroeder et al. teach the use of ABEI (see p. 433) as a useful label in competitive assays (see p. 424).

Therefore, it would have been obvious for a person of ordinary skill in the art at the time of invention to include in the method for assaying 25-hydroxy-vitamin D of Armbruster et al. and Romelli et al., the ABEI label, as taught by Schroeder et al., because Schroeder et al. teach that aminophthalhydrazides, including ABEI, are non-radioactive and consequently more convenient to handle and can be detected with high sensitivity compared to alternative labels (see p. 424).

Claims 15 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Armbruster et al. (US 6,787,660) in view of Romelli et al. (US 5,382,530), as applied to claims 1, 10 and 13, and further in view of Schroeder et al., 57 METHODS ENZYMOL. 424 (1978) and Geckeler, 1 POLYMER BULLETIN 427 (1979).

Armbruster et al. and Romelli et al. teach a method for assaying 25-hydroxy-vitamin D as substantially described supra. The aforementioned references do not teach the use of an ABEI tracer or a 2,2'-(Ethylenedioxy)diethylamine linker or a diamino C_3- to C_{12}- chain linker.

However, Schroeder et al. teach the use of ABEI (see p. 433) as a useful label in competitive assays (see p. 424), while Geckeler teaches the use of a 2,2'-(Ethylenedioxy)diethylamine linker (see p. 429) for attaching pharmacologically active compounds to other molecules (see p. 427).

Therefore, it would have been obvious for a person of ordinary skill in the art at the time of invention to include in the method for assaying 25-hydroxy-vitamin D of Armbruster et al. and

Romelli et al., the ABEI label, as taught by Schroeder et al., because Schroeder et al. teach that aminophthalhydrazides, including ABEI, are non-radioactive and consequently more convenient to handle and can be detected with high sensitivity compared to alternative labels (see p. 424). Geckeler teaches that 2,2'-(Ethylenedioxy)diethylamine linkers exhibit excellent solubility properties, which is useful for solubilizing drugs and other compounds that are relatively insoluble.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Armbruster et al. (US 6,787,660) in view of Romelli et al. (US 5,382,530), as applied to claims 1, 10 and 13, and further in view of Schroeder et al., 57 METHODS ENZYMOL. 424 (1978) and Zalipsky, 6 BIOCONJUGATE CHEM. 150 (1995).

Armbruster et al. and Romelli et al. teach a method for assaying 25-hydroxy-vitamin D as substantially described supra. The aforementioned references do not teach the use of an ABEI tracer or a polyethylene glycol linker.

However, Schroeder et al. teach the use of ABEI (see p. 433) as a useful label in competitive assays (see p. 424), while Zalipsky teaches the use of a polyethylene glycol linker to produce conjugates with low molecular weight compounds (see Abstract).

Therefore, it would have been obvious for a person of ordinary skill in the art at the time of invention to include in the method for assaying 25-hydroxy-vitamin D of Armbruster et al. and Romelli et al., the ABEI label, as taught by Schroeder et al., because Schroeder et al. teach that aminophthalhydrazides, including ABEI, are non-radioactive and consequently more convenient

to handle and can be detected with high sensitivity compared to alternative labels (see p. 424). Zalipsky teaches that polyethylene glycol linkers possess a wide range of solubilities (see Abstract), which is useful for improving the solubility of a compound of interest.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Armbruster et al. (US 6,787,660) in view of Romelli et al. (US 5,382,530), as applied to claims 1, 10 and 13, and further in view of Schroeder et al., 57 METHODS ENZYMOL. 424 (1978) and Hornby & Morris (US 4,115,305).

Armbruster et al. and Romelli et al. teach a method for assaying 25-hydroxy-vitamin D as substantially described supra. The aforementioned references do not teach the use of an ABEI tracer or a dimethyl adipimidate linker.

However, Schroeder et al. teach the use of ABEI (see p. 433) as a useful label in competitive assays (see p. 424), while Hornby & Morris teach the use of adipimidate linkers (see col. 2, line 44) for linking biomolecules.

Therefore, it would have been obvious for a person of ordinary skill in the art at the time of invention to include in the method for assaying 25-hydroxy-vitamin D of Armbruster et al. and Romelli et al., the ABEI label, as taught by Schroeder et al., because Schroeder et al. teach that aminophthalhydrazides, including ABEI, are non-radioactive and consequently more convenient to handle and can be detected with high sensitivity compared to alternative labels (see p. 424). Hornby & Morris teach that adipimidate linkers have reduced reactivity towards the reaction medium (see col. 1, lines 33-36), which results in less interference during immunoassays.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J Venci
Examiner
Art Unit 1641

djv

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

11/29/04